With an aging, cost-conscious, and health-minded population, the United States has become increasingly aware of medical issues. Advanced technology can address some of these issues, revolutionizing many medical procedures and enhancing the quality of medical products and services. Procedures that once were complex, painful, or risky are now, or will soon be, performed by innovative noninvasive or minimally invasive techniques. For example, advanced sensors will allow glucose levels in blood to be monitored without puncturing the skin, offering better quality of life for millions of diabetics. Sophisticated technology will offer physicians better, more accurate tools, potentially saving lives and improving the quality and efficiency of patient care. Also, such technologies often reduce or eliminate the need for hospital care, thereby reducing associated costs.

Today's market. The United States is the world leader in producing medical devices, accounting for 41 percent of the total worldwide market. The medical industry relies heavily on innovative breakthroughs provided by the 11,000 companies—most of which are small businesses—that contribute to its products. U.S. companies have developed more than 80 percent of all commercialized medical devices produced over the past 40 years. In 1993, the worldwide market for medical devices was roughly $93 billion.[1] The customers—hospitals, private practitioners, health maintenance organizations, and the patients themselves—have, until recently, been limited to traditional technologies used for years; however, innovative technologies with cost-saving implications are beginning to change this picture.

Tomorrow's opportunity. To protect the Nation and its troops overseas, BMDO has funded the development of many highly advanced technologies such as computer algorithms, lasers, and optics to detect and eliminate an enemy's incoming missiles. But the same technology can be used to protect the Nation from another enemy—the threat of disease. Many organizations with BMDO-funded R&D are applying their findings to the medical arena, making new breakthroughs in cardiac disease, cancer, and diabetes. The following section describes six of these innovations.

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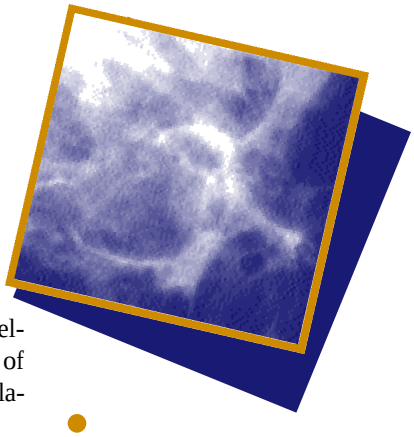
[1] *Industry Surveys,* Standard & Poor's, September 7, 1995, p. H-43.

Los Alamos National Laboratory, page 68

MEDICAL TECHNOLOGIES

X-Ray Detector For Cancer May Save Lives



Hughes Aircraft company and NOVA R&D are developing a device to detect breast cancer early, potentially saving thousands of lives.

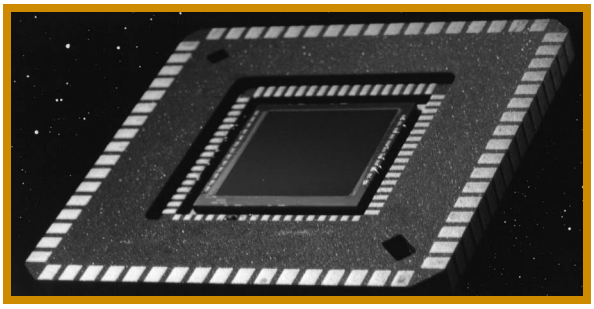
This year, 182,000 American women will be diagnosed with breast cancer; 46,000 will die from the disease. Many of these lives might have been saved had the cancer been detected sooner.[2] In fact, with early detection, 5-year survival rates are estimated at 96 percent. Unfortunately, early warning signs are missed more than half the time. Many women who develop breast cancer had received clean bills of health on previous mammograms; in 60 percent of these cases, cancer indications were visible in earlier tests but went undetected using the relatively low-contrast images available.

NOVA R&D, Inc. (Riverside, CA), and Hughes Aircraft Company (El Segundo, CA) have found a way to solve this problem. The team has come up with an advanced digital mammography unit that could help doctors spot life-threatening cancer early enough to save thousands of lives.

Using BMDO-funded R&D, NOVA is developing a mammography system through the National Institutes of Health.

This technology is based on BMDO funding at Hughes for work on silicon pixel x-ray detectors (SiPD). It was initially developed with military needs in mind, such as the Sensor Experiment Evaluation and Review (SEER), Precursor Above the Horizon Sensor (PATHS), and Hybrids With Advanced Yield for Surveillance (HYWAYS) programs.

NOVA has enhanced an SiPD device and is developing the mammography system with funding from a National Institutes of Health SBIR contract. In this system, researchers are mounting a linear detector array on an accurate swing arm so the array can be scanned under the patient's breast. Among other improvements, NOVA expects its system will be able to display images with greater contrast and finer detail than other methods of breast examination. It is also expected to expose patients to less radiation.



The silicon pixel device, pictured above, is the basis for the digital mammography unit. This device is being enhanced so that images can be displayed with greater contrast and finer detail than conventional mammography.

The technology has medical applications in addition to mammography. For example, it can be used for tomographic animal studies, bone densitometry, and panoramic dental x-rays. In fact, this technology looks so promising that Fischer Imaging (Denver, CO) has already expressed interest in helping to commercialize it once the project is completed.

About The Technology

The technology behind NOVA's SiPD device consists of two sections: a two-dimensional silicon p-doped/intrinsic/n-doped (PIN) diode array and a front-end readout electronics chip with time-delayed integration (TDI) charge-coupled device (CCD) function. This function, developed by NOVA, allows the system to tolerate random dead pixels in the array that may occur before or after fabrication. The sections are designed with matching pixel geometry and are electrically connected using an indium bump bonding technique. This allows each diode to be directly connected to its readout electronics and allows fabrication of small capacitance and low noise detectors.

Though Hughes holds a patent on the original technology, NOVA has enhanced it for medical imaging. In developing its own readout system, NOVA made the pixel array thicker and added the time-delayed integration function, resulting in a technology that promises to detect the warning signs of breast cancer before it is too late.

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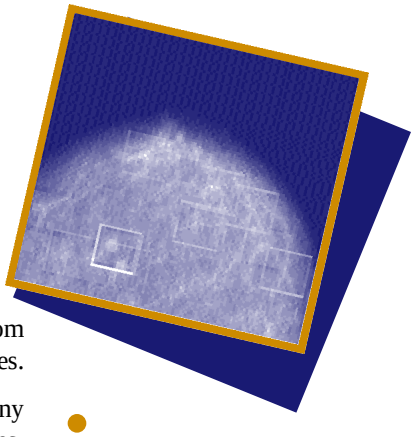
[2] *Cancer Facts* (Factsheet), American Cancer Society, 1994.

Pattern Recognition Speeds Detection Of Breast Cancer



Bold white boxes indicate possible abnormalities in this mammogram.

Costs for mammography services, estimated in 1992 to be as much as $3 billion in the United States[3], account for a large portion of medical expenses. When adapted to medical use, BMDO-funded research in pattern recognition technology can reduce these mammography costs by speeding analysis and diagnosis. This technology may also reduce the number of deaths from breast cancer, since it can detect the disease earlier than conventional mammography techniques.

Rose Health Enterprises (Denver, CO) and Lockheed Martin (Denver, CO) formed a company called MedDetect, LLC, to use such BMDO-funded technology to analyze medical images. MedDetect's optical system is projected to quickly identify 75 percent of screening mammograms that are negative, allowing doctors more time to examine potential cancer cases closely.

> MEDDETECT'S SYSTEM IS PROJECTED TO QUICKLY IDENTIFY 75 PERCENT OF SCREENING MAMMOGRAMS THAT ARE NEGATIVE, GIVING DOCTORS MORE TIME TO EXAMINE POTENTIAL CANCER CASES CLOSELY.

In addition, the technology makes screening a more powerful and accurate tool by automatically identifying abnormal image attributes. In preliminary tests on an archive of mammographic images, it has already detected a cancerous breast lesion, that, using conventional mammography, did not appear for another year.

MedDetect's initial work in the medical arena has been focused on integrating optical processors with complex algorithms to improve mammographic images. But the company expects to use these methods in other medical applications as well, such as to improve cancer detection processes in chest x-rays and Pap smears. It is using much of the technology, including target scene generation software and optical components for rapid data processing, that Lockheed Martin developed with BMDO funding for advanced target acquisition and recognition.

MedDetect's optical system will be compatible with "filmless" digital mammography, which several companies and research groups, such as Fischer Imaging (Denver, CO), NOVA R&D (Riverside, CA), and ThermoTrex (San Diego, CA) are developing. Using MedDetect's technology, digital x-ray images can be analyzed in less than a minute. The images can then be transmitted to another radiologist for a second opinion. In addition, digitally storing images at a central location allows physicians to quickly access records for baseline image analysis and comparison.

Both Rose and Lockheed Martin are providing seed money for MedDetect, with plans to raise additional private capital and have a prototype available within 18 to 24 months. Technology improvements achieved by MedDetect will also be returned to Lockheed Martin's defense technologies.

About The Technology

MedDetect's system is a hybrid of optical and digital processing. An optical correlator uses lenses and a low-power laser to examine the mammogram. The optical correlator, with programmable spatial light modulators and Fourier transform lens pairs, uses photons instead of electrons to perform the calculations to detect an abnormal feature. This information is then transmitted to a computer that uses neural network software to "learn" the specific attributes of breast abnormalities. The learned information is stored and applied to new images.

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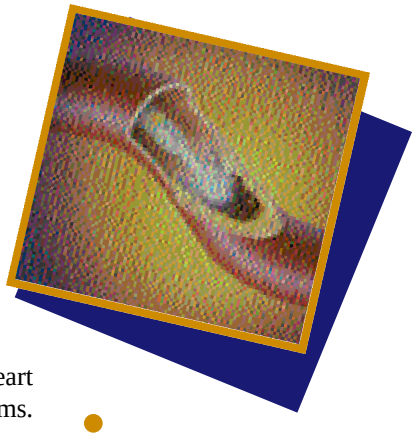
[3]How Much Preventive Care Can We Afford?…K. Terry; *Medical Economics,* August 23, 1993, p. 124.

Lasers Target Blood Clots In New Method



Laser thrombolysis, pictured above, destroys blood clots using a laser beam. This method presents cost, recovery time, and safety advantages over methods such as bypass surgery.

Coronary heart disease (CHD) is the leading cause of illness and death in the United States, with an estimated 52 million adults at moderate to high risk. The American Heart Association found that medical costs associated with treating this disease amount to $56.3 billion per year; lost productivity adds $8 billion to this cost.

CHD can lead to blood clots in coronary arteries, which impede blood flow and can cause heart attacks. While treatments are available to get rid of blood clots, they are not without problems. Therefore, medical researchers are seeking safer, easier, and cheaper ways to eliminate clots.

One approach is a technology called laser thrombolysis, which is being developed in a cooperative research and development agreement (CRADA) at Los Alamos National Laboratory, or LANL. The laboratory is working with medical experts from all over the Nation, including Palomar Medical Technologies (Beverly, MA), Oregon Health Sciences University (Portland, OR), and St. Vincent's Hospital (Portland, OR). Initiated in early 1995, the U.S. Department of Energy-funded CRADA is scheduled for 3 years of development.

In laser thrombolysis, a laser beam is delivered through an optical catheter, usually inserted in the femoral artery (in the thigh) and threaded into the affected artery of the heart, where a pulsed laser beam destroys the clot. Several years ago, BMDO funded related theoretical laser studies in laser-matter coupling at LANL, which were applied to laser pulses on biological tissue and helped provide insight into this medical technology.

The group is currently conducting Food and Drug Administration (FDA)-sponsored testing, a year-long process that involves 60 heart attack patients at St. Vincent's Hospital, Washington Hospital Center (Washington, DC), Scripps Clinic (La Jolla, CA), and Methodist Hospital (Lubbock, TX). Once developed, laser thrombolysis could annually treat more than 100,000 patients; but before this happens, the method needs to be further refined and FDA approved.

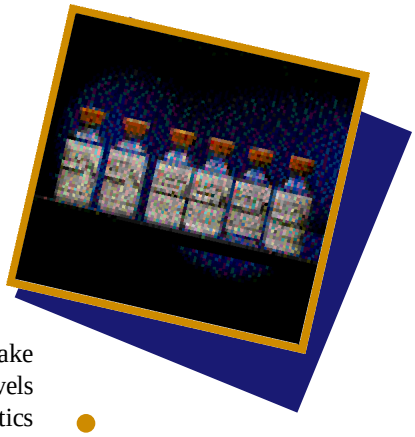
USING BMDO-FUNDED R&D, THE GROUP IS CONDUCTING FDA-SPONSORED TESTING TO ELIMINATE BLOOD CLOTS, A PROCESS THAT INVOLVES 60 HEART ATTACK PATIENTS.

Research findings indicate that laser technology has several advantages over other methods. For example, depending on the patient, laser thrombolysis may reduce the need for injections of clot-busting drugs such as streptokinase and tissue plasminogen activator (tPA), which enzymatically dissolve clots. Suitable for only about 40 to 70 percent of potential patients, these drugs sometimes cause allergic reactions and hemorrhaging. Laser thrombolysis has not been shown to cause such problems. In addition, since the thrombolysis technique is more selective in destroying the clot, it does not present problems associated with current angioplasty or other treatments, which can damage the artery walls. It also offers cost, recovery time, and safety advantages over bypass surgery, in which surgeons must replace arteries.

About The Technology

In laser thrombolysis, a laser beam is delivered to a blood clot through a fluid-core optical catheter. The yellow-green laser pulse delivered in the catheter is absorbed much more efficiently in a blood clot than in the surrounding arterial wall, which means that the clot can be heated and vaporized without damaging adjacent structures. The platelets in the clot are also destroyed, reducing the chance of a new clot forming from the released debris. Avoiding damage to the arterial wall is also important in the prevention of re-stenosis, or renewed narrowing. The laser thrombolysis procedure is monitored by radiography similar to more conventional angioplasty methods. Fortunately, because the x-ray-opaque dye used in these procedures is transparent to the laser beam's wavelength, the laser method is compatible with existing catheterization protocols.

Blood Glucose Monitor Eliminates Painful Testing



Roughly 15 million people in the United States suffer from diabetes.[4] In the realm of diseases, it is the third biggest killer and can lead to blindness, kidney failure, cardiovascular disease, and serious infection.

Therefore, it is essential for diabetics to maintain good health, which often requires them to take insulin every day. Today, about 2.5 million patients must carefully monitor blood glucose levels to determine the efficacy of the insulin. Unfortunately, current technology dictates that diabetics stick their fingers with a needle a few times each day to test their blood. This process is both painful and expensive—roughly $800 million is spent on home glucose kits each year.[5]

Roughly 2.5 million patients must monitor blood glucose levels to determine the efficacy of the insulin, daily sticking their fingers with a needle to test blood. Rio Grande Medical Technologies' device offers a noninvasive approach to this testing.

> NONINVASIVE BLOOD GLUCOSE MONITORS WILL BE A BOON TO THE HEALTH OF DIABETIC PATIENTS.

As a noninvasive, needle-free alternative, Rio Grande Medical Technologies, Inc. (Albuquerque, NM), is developing a glucose monitor that reads blood glucose levels using spectral analysis of a near-infrared (IR) beam. This innovation presents a painless and waste-free way to monitor blood glucose levels. If the cost and size can be reduced this technology may well extend glucose monitoring services to many more diabetics with less stringent insulin requirements.

The portable blood analyzer can also be used in law enforcement and emergency medicine, and for critical care patients and those undergoing general anesthesia. Forward medical care on the battlefield may be another use.

Rio Grande was founded expressly to commercialize this technology, collaborating extensively with Sandia National Laboratories, or SNL (Albuquerque, NM), and the University of New Mexico School of Medicine. BMDO-sponsored research at SNL led to the multivariate analysis software used in the monitor's spectral analyzer—R&D originally designed for space-based imaging and nondestructive analysis.

Rio Grande was founded expressly to commercialize this technology. Pictured above is the device, which uses spectral analysis of a near infrared beam.

Rio Grande is aggressively pursuing the technology development and product engineering with strong contributions from a large U.S. health care company and funding from the Advanced Research Projects Agency Technology Reinvestment Project. One of the challenges now is to reduce the size of the monitor.

About The Technology

To operate the blood monitor, a near-IR light beam is passed through the finger, and the spectral components of the emergent beam are measured using statistical computing and spectroscopic techniques. The level of glucose is determined by how much light at a particular wavelength is absorbed by the glucose compared with how much light strikes the photodetector. The monitor is nearly as accurate as present systems, which rely on visual or digital reading of color-coded strips compared with a blood sample. It eliminates finger-sticking, and can also provide a way to quickly examine trends in blood glucose levels. Near-IR spectral analyzers can also be used to determine blood alcohol levels, as well as carbon dioxide, bicarbonate ion, and oxygen content of the blood.

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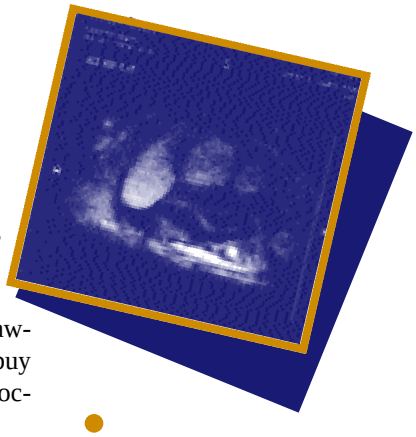
[4] *Draft Testimony to House Subcommittees on Basic Research and Technology,* Tom Fortin; Rio Grande Medical Technologies, Inc., presented June 27, 1995.

[5] Infrared Technology May Aid Diabetics, *Aviation Week & Space Technology*, August 23, 1993, p. 65.

Superconductors Reduce Time For MRIs

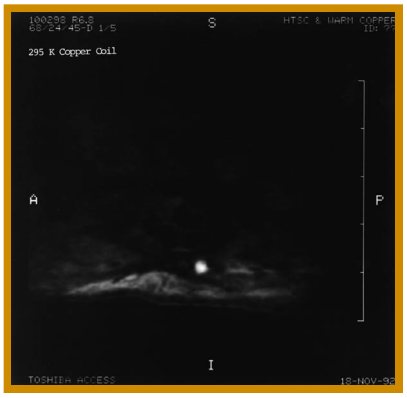


Pictured above is a magnetic resonance image using STI's superconducting coil. Pictured below is the same image obtained using conventional copper coils.

Magnetic resonance imaging has become almost as routine as the x-ray. MRI enables doctors to detect brain tumors, examine torn ligaments, and observe other soft tissues without having to open up the patient. But these imagers are not problem free. For example, patients must lie very still inside a costly and noisy capsule for about 40 minutes, which is a major drawback for children and people with claustrophobia—not to mention the hospitals that must buy these machines. And while "open" MRIs are available, they often cannot show the detail that doctors need for making crucial decisions.

To combat these problems, researchers at Superconductor Technologies, Inc., or STI (Santa Barbara, CA), are speeding up MRIs and improving their images using a high-temperature superconducting coil called the SuperSensor™ coil. Replacing copper coils used in open MRIs, STI's technology can produce images comparable to those of conventional MRIs in about a quarter of the time. And if doctors use an MRI with the SuperSensor™ coil for the traditional 40 minute time period, images with 50 to 150 percent better resolution can be produced.

> In 10 minutes, open-access MRIs using the SuperSensor™ coil will produce images comparable to those of conventional MRIs.



These benefits can occur in an open system, eliminating the cost and claustrophobia problems of closed systems. The Food and Drug Administration has approved one of STI's coils; and while approval is needed for two more to complete a system, the company has already overcome a major hurdle in entering the medical industry.

Through its SBIR program in high-temperature superconductor (HTS) thin films, BMDO funded the baseline developments that led to the SuperSensor™ coil. Since then, the National Institutes of Health has funded research to develop and reduce the costs of such coils for MRI applications. STI is interested in partnerships to bring this technology to market.

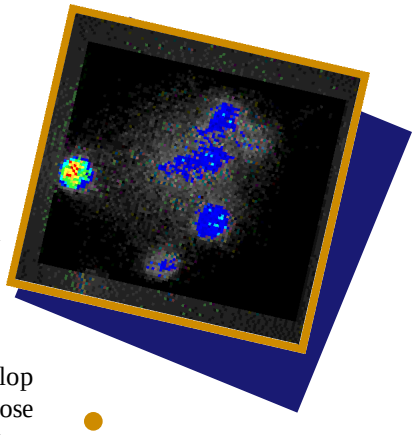
STI's commercialization of BMDO-funded R&D has also spread into other areas. In fact, the company has an entire product line called *Micro*Loss® for microwave communications, which includes superconducting thin films, superconducting microwave resonators, superconducting custom design kits, and hi-Q superconducting microwave resonators (2 to 35 gigahertz). The company's technology is also preventing dropped cellular telephone calls by incorporating HTS thin-film components into cellular telephone base station receivers, making them more sensitive and accurate in handling calls. STI is filling orders from three major cellular communications companies for HTS receiver filters.

About The Technology

One of the hurdles in manufacturing an HTS thin film is finding a substrate compatible with the superconducting material. The substrate should support the HTS material and be a good electrical insulator. In addition, the crystal lattice of the substrate should align closely with the lattice of the crystallized HTS material. This alignment allows maximum flow of current through the thin film.

To meet these requirements, STI has developed a thallium barium calcium copper oxide (TBCCO) superconducting thin film deposited on a lanthanum aluminate ($LaAlO_3$) substrate. TBCCO is advantageous because it will superconduct up to the relatively high temperature of 100 K (–279ºF). $LaAlO_3$, in turn, has a high dielectric constant (about 24) and a low loss tangent (3×10^{-5}), both of which indicate the material's ability to electrically insulate. The substrate's good insulating qualities make the superconducting system highly efficient.

Tunable Filters Adjust To Many Wavelengths



Ciencia's AOTF technology helps visualize fluorescence activity in living cells.

As health care moves into the 21st century, innovations in optical technologies are expected to change the way doctors and other medical personnel do their jobs, both in the operating room and on the examination table. Such advances will, for example, allow doctors to analyze blood without drawing a drop.

Researchers at Ciencia, Inc. (East Hartford, CT), have used BMDO-funded technology to develop optical filters that may contribute to this change, vastly improving the way doctors diagnose patients and analyze blood and tissue. Their patented polymer-based acousto-optic tunable filters (AOTFs), originally developed for defense, are being used in rugged, portable, low-cost spectrometers for the medical community.

Although several companies have developed AOTFs, Ciencia's innovative approach makes the manufacture of these devices easier and more reliable, bringing them much closer to commercial use. To move its spectrometers to market, Ciencia has been funded by Connecticut Innovations, Inc., a State-funded commercialization organization.

Ciencia staff began work on AOTFs while at Scientific Research Associates, Inc. (Glastonbury, CT), for the BMDO SBIR program. They later spun off and formed Ciencia, developing AOTF-based ultraviolet sensors for military target identification and surveillance systems. Ciencia has since received BMDO SBIR funding for further research and development of AOTF technology.

> CIENCIA'S RUGGED, PORTABLE SPECTROMETERS CAN IMPROVE THE WAY THE MEDICAL COMMUNITY DIAGNOSES PATIENTS AND ANALYZES BLOOD AND TISSUE.

One of the products Ciencia is developing with funding from the National Institute of Mental Health is a portable cancer-detecting spectrometer. Able to analyze tissue in vivo, this product could be key in optical biopsy systems, which use light absorption measurements to detect cancer—a painless alternative to surgical biopsies. Ciencia's Raman spectrometer will allow doctors to distinguish between malignant cells and benign tissue by analyzing biological fluids and examining their fluorescence and Raman signatures. Researchers at the company are also developing filters that can determine cell contents, with future plans for blood flow imaging.

In addition to medical applications, Ciencia is pursuing markets for environmental technologies, chemical process control, and remote sensing. For example, working with Sunkist Growers, Inc., Ciencia has completed the first phase of an optical nondestructive testing system that detects molds and other contaminants in citrus fruit.

The company is also planning a collaboration with Woods Hole Marine Biology Laboratory to design sensors that can measure chlorophyll content in phytoplankton. Such measurements can yield valuable qualitative and quantitative information about the habitat and population size of tuna, dolphins, and other surface-dwelling fish and mammals. Scientists currently assess these populations visually through aerial inspection—a method somewhat imprecise.

About The Technology

Acousto-optic devices use ultrasound to alter the refractive index of an optical medium, typically a crystal. Ciencia's AOTF is based on an organic amorphous material rather than the more conventional inorganic crystals. The organics are less expensive to make than the crystals, allow for uniformity and quality control during the manufacturing process, and permit independent control of bandpass and bandwidth. Unlike an ordinary monochromator, the AOTF can be tuned electronically, so it has no moving parts. By sweeping the ultrasonic tuning frequency, the polymeric device produces spectrally resolved images.